

# NAVAL HEALTH RESEARCH CENTER

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## ***TWO FATAL CASES OF ADENOVIRUS-RELATED ILLNESS IN PREVIOUSLY HEALTHY YOUNG ADULTS – ILLINOIS, 2000***

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## **MORBIDITY AND MORTALITY WEEKLY REPORT**

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### **Two Fatal Cases of Adenovirus-Related Illness in Previously Healthy Young Adults — Illinois, 2000**

Adenoviruses are common pathogens that often are associated with respiratory and gastrointestinal illness and/or conjunctivitis in young persons. Adenovirus serotypes 4 and 7 have caused outbreaks of self-limited febrile respiratory illness in young adults in basic military training. During the 1950s and 1960s, up to 10% of recruits were infected with adenovirus, and these pathogens were responsible for approximately 90% of pneumonia hospitalizations (1). Beginning in 1971, all military recruits received oral, live, enteric-coated vaccines that were licensed by the Food and Drug Administration as safe and effective in preventing illness from adenovirus serotypes 4 and 7. In 1996, the sole manufacturer ceased production of adenoviral vaccines and, as supplies dwindled during the next few years, outbreaks of adenoviral respiratory illness reemerged in military settings (2). Since 1999, approximately 10%–12% of all recruits have become ill with adenovirus infection in basic training, similar to the prevaccine era. This report describes the first two deaths probably associated with adenovirus infection identified in military recruits since the vaccines became unavailable. The military has requested proposals for a new adenovirus vaccine manufacturer; however, these deaths suggest that efforts by policymakers and pharmaceutical companies to reestablish adenoviral vaccine production should be intensified.

#### **Case Reports**

**Case 1.** A healthy 21-year-old man arrived at Navy basic training in Great Lakes, Illinois, on May 19, 2000. His medical history was negative for underlying illnesses. He took no medications and denied alcohol or tobacco use. Within one week of arrival, he received several standard vaccinations, including meningococcal vaccine. On June 20–23, he presented to the medical clinic with upper respiratory symptoms. His clinical evaluations did not suggest severe illness, and two bacterial throat cultures were negative. On June 23, he was prescribed a 5-day course of azithromycin for suspected bronchitis. On June 24, he was found unconscious in the barracks. He was transported to a local hospital where he had tonic clonic seizures and respiratory failure that required a ventilator. A chest radiograph revealed a right upper lobe infiltrate, and computer tomography of the head was positive for sinusitis. Examination of cerebrospinal fluid revealed elevated protein levels, but no identifiable pathogens. Blood cultures were negative. He was treated with broad-spectrum antibacterial agents (i.e., vancomycin, ceftriaxone, and metronidazole) and antivirals (i.e., acyclovir and foscarnet). He did not regain consciousness and he died on July 3 from complications of encephalitis.

*Adenovirus — Continued*

Autopsy findings included histologic changes in the brain and spinal cord consistent with viral encephalitis. Both lungs showed bronchiolitis obliterans and organizing pneumonia. Cultures, special stains, and electron microscopy of autopsy specimens did not identify specific pathogens. Molecular testing by polymerase chain reaction (PCR) assay of lung and brain tissue was positive for adenovirus DNA using multiple primer sets (3,4). Analysis of premorbid and postmortem serum specimens showed a greater than fourfold rise in neutralizing antibody titers to both adenovirus types 4 and 7.

**Case 2.** A healthy 18-year-old man arrived at Navy basic training in Great Lakes, Illinois, on August 1. He took no medication and did not use tobacco products. Within one week of arrival, he received several standard vaccinations and benzathine penicillin G (1.2 mu intramuscularly) as prophylaxis for group A streptococcal infections. On August 17, 29, and September 17, he presented to the medical clinic with upper respiratory symptoms. Examinations disclosed no severe illness; he was given acetaminophen and decongestants. On September 18, he presented to the medical clinic with severe dyspnea, weakness, and a petechial rash on the legs. A chest radiograph identified multilobar infiltrates, and he was admitted to a local hospital where his condition rapidly deteriorated. He was given intravenous ceftriaxone and erythromycin and respiratory and hemodynamic support. He died 9 hours after admission with a clinical diagnosis of acute respiratory distress syndrome.

A culture of expectorated sputum collected the day of admission was later positive for group A streptococcus. An autopsy revealed diffuse hemorrhagic pneumonia and diffuse alveolar injury. Cultures and special stains of autopsy materials failed to identify specific pathogens. Electron microscopy indicated intracellular cocci in leukocytes of the lung tissue; no viruses were identified. PCR testing of lung tissue was positive for adenovirus DNA at two laboratories using multiple primer sets (3,4). Serologic studies were not performed.

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**Editorial Note:** These cases illustrate that severe morbidity and mortality are possible from adenovirus infections in previously healthy young adults. Serious adenoviral infections were reported in the U.S. military before vaccines were developed (5) and in unvaccinated civilians (6,7). In 1996, disease surveillance was established in response to impending loss of vaccine in the military.

Case 1 demonstrates the rare manifestation of central nervous system involvement by adenovirus. Although the serotype is impossible to identify, serotype 7 has been associated most commonly with meningitis and encephalitis (8). Surveillance has shown serotype 7 adenovirus as a pathogen identified among the approximately 30 new cases of respiratory illness seen at this training site each week (2); the number of cases of illness was slightly higher when the case 1 recruit was in training.

*Adenovirus — Continued*

Because the pathogen was not detected until postmortem examination, case 2 may have been an occult adenovirus infection. The clinical course met the criteria for probable streptococcal toxic shock syndrome, with hypotension, rash, acute respiratory distress syndrome, and group A streptococcus isolated from a nonsterile site (9). Adenovirus may not have been the primary source of illness but a co-morbidity factor (10).

In both cases, the postmortem diagnosis of adenovirus was made on limited evidence; PCR and serology indicated the presence of adenoviruses in case 1, and PCR alone was the basis for adenoviral detection in case 2. Isolating adenovirus in culture would have been stronger evidence of infection, but negative culture results can be expected when only postmortem specimens are available. The lack of adenovirus changes on electron microscopy may have been the result of the low sensitivity of this technique on limited tissue samples. Despite these limitations, the viral changes on autopsy, lack of identification of other viral pathogens, and PCR evidence support the diagnoses of adenovirus-related illnesses.

These are the first two deaths probably associated with adenovirus infection in the U.S. military since 1972. Until vaccines become available again, support should be given to ongoing surveillance efforts with appropriate laboratory techniques to identify adenoviral infections. Approximately 200,000 young persons begin U.S. military enlisted careers each year; therefore, clinicians should consider adenovirus infection in severely ill young persons in the military. Policymakers and pharmaceutical companies should consider reestablishing adenovirus vaccine production.

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